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13 MAR 1992

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Form 1/77

Patents Act 1977

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1 Please give the title of the invention: Imaging Method and Apparatus

❷ Applicant's details

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2a If you are applying as a corporate body please give:

Corporate name

Country *(and State of incorporation, if appropriate)*

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2[redacted] and 2f: *If there are further appl[redacted] please provide details on a separate sheet of paper.*

❑ **Second applicant** ***(if any)***

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4 Agent's or applicant's reference number *(if applicable)* 230P65431

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5 Are you claiming that this application be treated as having been filed on the date of filing of an earlier application?

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Claim(s)	3	Description	17
Abstract	1	Drawing(s)	4 (Informal)

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IMAGING APPARATUS AND METHOD

The present invention relates to an imaging method and an apparatus for performing same. In particular, it relates to a new method for making a type of image of the living mammalian body such as of a human. The resultant image is hereinafter referred to as a neurogram and shows the branching pattern of the peripheral, autonomic or cranial nerve tree so that it stands out in isolation from other structures.

Although many techniques have been developed for showing distinctive images of the brain, spinal cord, and spinal roots within the spinal canal, hitherto there has not been a successful method for creating images of the peripheral and cranial nerves as they pass among bones, muscles, lymphatics, tendons, ligaments, intermuscular septa, collections of fatty tissues, air or fluid spaces, veins, arteries, joints, skin, mucous membranes and other tissues. The peripheral, autonomic, and cranial nerves are relatively small compared to many other bodily tissues, and they often travel in bundles near other structures of comparable size and shape.

The lack of a suitable method for creating a distinct image of the nerves in a living mammal or human has been a great hindrance to physicians, surgeons, athletic trainers, pain treatment specialists. Such a neurogram would also be of great advantage to designers of ergonomic furniture, specialized body suits, boots, and various kinds of electronic or electric medical equipment which can be best used when the positions of nerves can be precisely located in advance.

Although many nerves travel along straight and simple

courses, there are very complex nerve arrangements such as the brachial plexus, lumbar plexus, or sacral plexus where bundles of nerves collect together, separate, rejoin, intermix, and resegregate in such a way as to create a very intricate three dimensional pattern. A compression or irritation of a small area of nerve within such a plexus (e.g. in the shoulder) can cause pain, numbness, weakness or paralysis at some distant site (e.g. in one finger). Even when a surgeon attempts to expose and examine the brachial plexus for direct inspection, the anatomic complexity can prove overwhelming, rendering surgery in this area to be extremely difficult and dangerous.

Unpublished co-pending PCT Patent Application No. PCT EP 91/01780 describes a method which attempts to make nerves stand out in images by the means of administering pharmaceutical agents which give the nerves special imaging properties. These pharmaceuticals are two-part agents which gain entry into and are transported within nerves where the second part of the agent has an imageable property.

If the second part of the molecule has elements with high nuclear density, then it may tend to increase the contrast of the nerve upon X-ray or Computed Tomography (CT) examination.

If the second part has a radioactive (e.g. positron emitting) element, then the nerve may be visible upon Positron Emission Tomography (PET) scanning, or if the second part has a magnetically active component, then the signal of the nerve may be changed upon Magnetic Resonance Imaging (MRI). These agents are injected into muscle and thereby used selectively to alter the imaging characteristics of the nerve supplying that muscle.

The main limitation with these pharmaceutical agents is that they can generally be used only to image a single nerve or nerve group. The MRI agents for nerve imaging actually gain their effect by blacking out the nerve in the image. Since nerves are difficult to see in current types of MRI images, the action of these MRI nerve imaging agents can be difficult to interpret.

The present disclosure relates to a new method, which quite remarkably, is capable of generating a three dimensional image of an individual patient's nerves and nerve plexuses. These images are acquired in such a way as to make all other structures in the body seem to tend to disappear so that only the nerve tree remains to be seen.

Thus, a first aspect of the present invention provides a method of selectively imaging neural tissue of a subject without use of neural contrast agents, the method comprising subjecting part of the subject anatomy to magnetic resonance imaging fields, detecting magnetic resonance and producing an image of neural tissue from said electronic signal so that in said image, a nerve, root or neural tract of interest can be visually differentiated from surrounding structures.

Preferably, the image selectivity is provided by discriminating water diffusion anisotropy as will be described in more detail hereinbelow.

A second aspect of the present invention provides a method of imaging neural tissue of a subject, the method comprising subjecting part of the subject anatomy to magnetic resonance imaging fields adapted to discriminate anisotropy of water diffusion, detecting magnetic resonance to produce an electronic signal in accordance with said resonance and producing an image of neural tissue from said electronic signal.

Neurographic imaging effected in accordance with the present invention utilises a set of special pulse sequence and program instructions to control the electronic equipment of an MRI scanner. For the imaging of fine nerve branches, the pulse sequences are aided by the use of special signal and imaging coils placed near or around the portion of the body of greatest interest. This does not require the administration of any pharmaceutical agent. Indeed, since neurographic imaging makes nerves appear bright and isolated in an image, it then becomes far more informative to selectively black out one of the nerves by means of administering an intraneural pharmaceutical contrast agent.

Thus neurography can be viewed as a way of effecting a process which rapidly produces an image of an entirely new kind, wherein that image can be examined for its anatomical information content, and wherein that image can be manipulated by the administration of pharmaceutical agents.

The aforementioned nerve imaging pharmaceutical agents were designed to help in the diagnosis of nerve compressions and nerve compressions and nerve injuries, it was not anticipated that the nerves could be seen in relative isolation without administering any pharmaceutical. Indeed, users of such agents have acutely appreciated the need for some imaging technique which would synergistically render the effects of the intraneural agents into much more useful form, although neurography <u>per se</u> had not been appreciated as the solution to this problem, nor had any proposal to attempt to accomplish neurography been made.

The fine spatial resolution required for creating detailed images of peripheral nerves, including their

small distal ramifications and divisions, is well within the physical range of current clinical magnetic resonance imaging instruments, particularly when specially designed local signal and imaging coils are used.

The inventors have discovered that there are various different sets of pulse sequences and combinations of pulse sequences which can be used to unambiguously distinguish small nerves from neighbouring structures of similar shape and location. This includes the combination of some existing sequences into new groupings for use in new situations as well as the design of new sequences which incorporate optimized features for the purpose of neurographic imaging.

The ideal 'neurographic image' is analogous to a subtraction angiogram (an image showing only blood vessels), but sharply highlights a nerve rather than a vessel. Such an image is most useful for confirming the identification of nerves in a given imaging plane as well as for locating nerve injuries and nerve compressions.

The inventors have carried out experiments in which they tested imaging techniques which enabled them to selectively delete the signal from non-neural structures and also evaluated techniques which permitted relative enhancement of the image signal from nerve. One discovery was that neurographic imaging could be greatly aided by taking special advantage of the "anisotropic water diffusion" which is known to take place in muscle, in the central nervous system and in peripheral nerves. Stated simply, water diffusion occurs preferentially along the axial length of nerves, more than radially across the nerve tissue. This directional preference for diffusion may be detected by magnetic resonance

imaging, more especially by proton nmr imaging. However, nmr utilising other magnetic resonance susceptible nuclei may also be used, e.g. fluorine 19, carbon 13 phosphorus 31, deuterium or sodium 23.

The inventors have demonstrated that, under ideal image collection and pulse sequence circumstances, the diffusion coefficient of anisotropy in peripheral nerve is greater than that in muscle, and that it was possible to collect appropriate diffusion weighted images in such a way as to generate neurograms.

In the imaging method according to the present invention, it is preferred that magnetic diffusion weighted field gradients are applied in at least two different directions and the signals from the respective resultant resonances are subtracted to produce said discrimination of water diffusion anisotropy.

Most preferably, the magnetic field gradients are applied in mutually substantially orthogonal directions.

To enhance the image of the nerves, it is preferable to apply a process to eliminate non-neural signals during the magnetic resonance imaging, for example by suppression of resonance signals from fat.

Fat suppression may for example be effected by chemical shift selection or by selective water stimulation.

Elimination of non-neural signals may also be effected by magnetisation transfer.

The present invention also includes a method of diagnosis or physiological investigation comprising application to a part of the subject anatomy of an imaging method according to the present invention as hereinbefore described.

Various diagnostic applications of the method of the present invention may be better understood with reference to Figure 1 of the accompanying drawings, which shows a sectional view through a vertebra. The structures and conditions illustrated are denoted by the following reference numerals:-

9. Herniated Disk
10. Compressed Root
11. Spinous Process
12. Anulus Fibrosus
13. Nucleus Pulposus
14. Autonomic Ganglion
15. Ventral Root
16. Ventral Ramus
17. Transverse Process
18. Dorsal Ramus
19. Dorsal Root Ganglion
20. Facet
21. Dorsal Root
22. Extradural Fat
23. Root in Cauda Equina
24. Dural Sac
25. Cerebrospinal Fluid within Dual Sac.

Such diagnostic applications include the following:-

1. Demonstrating the anatomy of peripheral, cranial, and autonomic nerves and nerve plexuses.

2. Demonstrating the anatomy of spinal roots, particularly, cervical, thoracic or lumbar spinal roots where they pass through fat at the foramina through which they exit the spinal canal.

3. Demonstrating the anatomy of spinal roots within the lumbar canal where they pass through quantities of extradural fat.

4. Demonstrating nerve, plexus or root compressions or injuries where abnormal changes in the direction, position, or other diffusional properties are caused by an injurious process, such as nerve transection, demyelinating diseases, peripheral neuropathies and crash injuries. These concerns apply similarly to

monitoring the regrowth of nerves.

5. Exploring the location of tumours or other masses within the spinal cord where it is useful to know the position of cortico-spinal motor tracts or other functional white matter long tracts relative to some abnormality.

6. Demonstrating the anatomy of the optic nerve, an extension of the brain, where it passes through the peri-orbital fat other fat on its route to the retina.

7. Tract tracing within the brain in order to provide useful images for study by radiologists, surgeons or physicians. In particular, for identification of the location of areas of 'eloquent cortex' such as the motor strip, or speech related areas. This method involves the spatial identification of relevant areas of the thalamus and then following projecting tracts to the area of interest on the cortical surface, or identify regions of interest by reference to their connections with other areas on the cortical surface.

8. Tracing of nerves as they pass through tumours of low diffusional anisotropy. Such as the passage of the VIIth nerve through an acoustic neuroma in order to permit a surgeon to know the location of the nerve in or near the tumour and so to have the ability to avoid the nerve during surgery on the tumour.

9. Application of diffusion anisotropy imaging for the evaluation of diffuse axonal injury, as may occur in head injury.

The first aspect of the invention also provides an apparatus for selectively imaging neural tissue of a subject without use of neural control agents, the

apparatus comprising means for subjecting part of the subject anatomy to magnetic resonance fields, means for detecting magnetic resonance to produce an electronic signal in accordance with said resonance and means for producing an image of neural tissue from said electronic signal so that in said image, a nerve root or neural tract of interest can be visually differentiated from surrounding structures.

The second aspect of the present invention also finds expression as an apparatus for imaging neural tissue of a subject, the apparatus comprising means for subjecting part of the subject anatomy to magnetic resonance fields adapted to discriminate anisotropy of water diffusion, means for detecting magnetic resonance to produce an electronic signal in accordance with said resonance and means for producing an image of neural tissue from said electronic signal.

Preferably, any apparatus according to the invention also comprises a coil for application of a radiofrequency field to said anatomy part and/or for detection of a resonance signal, wherein said coil is configured and dimensioned to fit closely over said anatomical part.

Conveniently, the coil is a solenoid coil or surface coil and is configured and dimensioned to fit closely over a human limb, shoulder, chest, pelvic region, neck or back.

In principle, selective imaging of part any other object or subject may be effected using magnetic resonance if that subject or object exhibits diffusion anisotropy in any part thereof. Thus, in medicine, for example a part of the cardiovascular system could be imaged in similar fashion. However, the technique could also be applied to rock strata, plants etc if diffusion anisotropy occurs in same.

Thus a third aspect of the present invention provides a method of selective imaging, the method comprising observing diffusion anisotropy.

The third aspect of the invention also provides a magnetic resonance apparatus for selective imaging, said apparatus being adapted to discriminate diffusion anisotropy.

The present invention will now be explained in more detail by the following description of a preferred embodiment and with reference to the accompanying drawings, in which: -

Figure 1 shows a section through a vertebra;

Figure 2 shows a magnetic resonance imaging apparatus for use in accordance with the present invention;

Figure 3 shows an example of pulse sequencing for operating the apparatus shown in Figure 1;

Figure 4 shows a diagram of transverse section of the upper fore-arm of a rabbit based on the fat suppressed image shown in Figure 5. 201) triceps muscle, 202) ulnar nerve, 203) brachial veins, 204) median nerve, 205) radial nerve, 206) humerus, 207) cephalic vein, 208) biceps muscle;

Figure 5 shows a fat suppressed image in which black represents highest intensity of resonance signal;

Figure 6 shows the effect of application of a perpendicular pulsed gradient renders the nerves as the highest intensity features in the image; and

Figure 7 shows the effect whereby reorienting the gradient parallel to the long axis of the nerve has a relatively greater effect in reducing the nerve signal than that of

the muscle.

Figure 2 shows an example magnetic resonance imaging apparatus 101 suitable for use in the present invention. It comprises a magnet 103 and a tuned radiofrequency (rf) coil 105 for excitation of the nucleus and detection of the required signal (separate transmit and receive coils may also be used). This coil is placed over a limb 107 under investigation.

One pair of a set 109, 111 of three pairs of coils used to generate a magnetic field gradient over the sample region. A computer 113 is used to control and synchronise the necessary electronic devices of the MRI and process to display the acquired data. An interface bus 115 is arranged between the computer and the electronic devices. A device 117 is used to generate the required radiofrequency pulse shapes. Another device 119 is used to generate the required gradient pulse shapes.

The device 117 is connected to a high power radiofrequency amplifier 121 for the rf pulses. Another amplifier 123 (one of three) is connected to the device 119 and has an output arranged to drive the gradient coils.

A duplexer 125 is arranged to steer the high power rf pulses from amplifier 121 to the coil 105 and steer the very low signals received by the coil to a preamplifier 127 for the received NMR signals. A mixer 129 is connected to the preamplifier to transform the high frequency nmr signals to low frequency signals by mixing with signals from a digitally controlled rf oscillator 131. The output of the mixer is connected to an analogue-to-digital converter 133 via a low pass filter 135.

Operation of the apparatus shown in Figure 2 to perform an

imaging method according to the present invention may be understoon better from the pulse sequences illustrated, by way of example only, in Figure 3.

Frequency selective pulses A, B and C selectively excite the nuclear spins of the fat molecules and the gradient pulses a, b, and c (along axes X, Y and Z respectively) dephase these spins thereby minimising the contribution of the fat signals to the final image. This is the known fat suppression technique using CHESS (Chemical Shift Selective) pulses.

A spin echo signal F, is generated by the combination of the radio-frequency excitation pulse D and refocussing pulse E. The pulsed gradients d to g are the imaging gradients used to encode the signal F in the usual manner such that an MRI image may be constructed. The sequence may be used to generate images from contiguous slices of the sample/patient under investigation.

The echo signal F, and therefore the pixel intensity in the constructed image is made sensitive to the spatial diffusion of the water molecules by the addition of the pulsed gradients h and h′ known as the "diffusion sensitizing gradients". Spatial anisotropy in the molecular diffusion is determined by comparing two or more images acquired with the diffusion sensitizing gradients oriented along different axes. The images are obtained in such a way to minimise motion artefacts by acquiring the data for the different diffusion sensitizing gradients in an interleaved manner.

In the case of a major axis of known diffusion anisotropy (eg. a nerve tract) a simple 'neurogram' may be generated by simply subtracting the appropriately scaled image obtained with the diffusion sensitizing gradient oriented parallel to the nerve tracts from a scaled image obtained

with the diffusion sensitizing gradient oriented perpendicular to the nerve tracts.

If the major axis of diffusional anisotropy is not known, a plurality of images are acquired with different orientations of the diffusion sensitizing gradients. The image data can then be processed to give a parameter associated with each pixel (or voxel in a 3D data set) which is a measure of the diffusional anisotropy at that point.

The method used in this embodiment first carries out the fat suppression technique which maintains excellent image resolution, or to use a sequence which selectively exciates only the water signal so that fat does not contribute to the final image and then, within the same pulse sequence, to include an oriented pulsed gradient for selective incorporation of information from diffusion anisotropy.

The various parts of the pulse sequence are selected so as to optimally destroy as many other signals as possible other than that of nerve as shown in Figure 7. Then, a second sequence is carried out which selectively destroys the nerve signal as by for instance, rotating the diffusion gradient orientation to be parallel rather than perpendicular to the nerve as shown in Figure 8.

The effect of these manoeuvers is to produce two images, the first of which shows up the nerve relatively brightly, and the second of which selectively destroys the nerve signal. When these two penultimate images are then mathematically or photographically, or optically subtracted from one another, and optionally divided by the signal information from a fat suppressed T2 weighted spin echo sequence (e.g. using the aforementioned CHESS technique), the result is the neurogram.

An alternative approach would be to use pulsed gradients oriented in each of a plurality of or into specially created axes suitable to the imaging task. In this fashion, it is possible to determine a parameter which characterised the diffusion coefficient anisotropy for each voxel in the image, including both magnitude and direction. This parameter can be rendered to produce a neurographic image for good image registration.

To optimize the technique where data processing requires the manipulation of the image data on a point by point basis between a plurality of image data sets, the image sequence can be modified to interleave the different sequences and so to minimise any motion artefact which could degrade the accuracy of the final image when the different sequences are collected at times separated by several minutes. Furthermore the image sequence can be synchronised to respiration or to the heartbeat to additionally reduce the effects of motion. It is also possible to carry out the signal acquisition using a so called "three dimensional" imaging sequences processed by using a 3D Fourier transform.

Images were obtained with a 4.7 Tesla, 33cm bore SISCO system fitted with a 10 Gauss/cm high performance auxiliary gradient insert (12 cm inner bore). A three-turn solenoid coil (2.5 cm in length and 3cm in diameter) was placed around the upper portion of the forelimb of 2 - 2.5 kg rabbits. The animals were maintained under balanced continuous intravenous infusion of an anaesthetic mixture containing 1 mg of medazolam, 1.5 mg of fluonisone and 50 μg of fentanyl per ml at rates of 4 to 10 ml/hr to achieve a deep anaesthesia minimising motion artefacts from respiration.

A specially modified multislice spin echo imaging sequence (TE=40 ms, TR=1 sec) was adjusted to provide fat

suppression (CHESS) and to accommodate diffusion weighting of images. This set of modifications allows operator control of the strength of the gradients and allows various strengths and orientations to be inserted into 'slots' or reserved times within the common base sequence. After an initial image with fat suppression only, there is next collected one image with diffusion gradients perpendicular to the image plane and then one image with diffusion gradients parallel to the image plane.

The CHESS sequence consisted of a 3 millisecond (ms) gaussian pulse for selective excitation of fat followed by a 5 Gauss/cm dephasing gradient of 3 ms duration performed 3 times with orthogonal gradients prior to each spin echo sequence. For diffusion weighting, pulsed gradients of strength G_i=10 G/cm, duration δ=7 ms, and separation Δ=20 ms, were symmetrically placed about the 180° pulse. Transverse images (nerves primarily orthogonal to image plane) with slice thickness of 2 mm were obtained for a 4 cm field of view with 256 phase encoding steps. Image data was zero filled to 512 points to give 78μm in plane resolution.

Simple spin echo images of limb anatomy proved inadequate for definitive identification of peripheral nerves because the nerves are typically surrounded by the high intensity signal from fat deposits in the intermuscular spaces. Further, there are a variety of structures similar to nerve in size and shape which follow similar routes.

However, it was found that the fat surrounding nerves is actually beneficial for nerve identification, because in a fat suppressed image, a relatively high intensity nerve signal stands out sharply within the very low intensity space left behind by the suppressed fat signal as shown in Figure 5.

Under these conditions the phenomenon of diffusion anisotropy was applied to the problem of nerve image enhancement and shown to be exceedingly effective (see Figure 4 to 7). Apparent diffusion coefficients perpendicular and parallel ($D_{\perp}$, $D_{\parallel}$) were calculated from average pixel intensity measurements over the region of interest (ROI) from each of the three different images in a given set. Calculation employed the formula (Intensity = $A_0 . \exp[-TE/T_2] . \exp[-bD]$, attenuation factor
$b=\gamma^2 G_i^2 \delta^2 [\Delta-\delta/3] = 61.9\ 10^3$
sec/cm^2).

Apparent Diffusion Coefficients (10^{-5} cm^2/sec)

	Muscle	Median Nerve
$D_{\perp}$	1.2	0.98
$D_{\parallel}$	1.8	2.3
$D_{\parallel}/D_{\perp}$	1.5	2.35

This example demonstrates that fat suppresion by CHESS enhances the visualization of peripheral nerves so that when different diffusion gradient orientations are incorporated in secondary segments of the imaging pulse sequence, the ultimate yield is a far larger relative change in intensity in the nerve signal than in muscle.

This intensity change then provides the basis for an image subtraction technique to achieve relative nerve image enhancement. The various subtracted or divided nerve images are then assembled mathematically by routine reconstruction techniques into a three dimensional image. Thus the objective of assembling three dimensional

neurograms is conveniently achieved.

In the light of this disclosure, modifications of the described embodiment, as well as other embodiments, all within the scope of the present invention as defined by the appended claims, will now be apparent to persons skilled in the art.

CLAIMS

1. A method of selectively imaging neural tissue of a subject without use of intraneural contrast agents, the method comprising subjecting part of the subject anatomy to magnetic resonance imaging fields, detecting magnetic resonance to produce an electronic signal in accordance with said resonance and producing an image of neural tissue from said electronic signal so that in said image, a nerve or root or neural tract of interest can be visually differentiated from surrounding structures.

2. A method of selectively imaging neural tissue of a subject, the method comprising subjecting part of the subject anatomy to magnetic resonance imaging fields adapted to discriminate anisotropy of water diffusion, detecting magnetic resonance to produce an electronic signal in accordance with said resonance and producing an image of neural tissue from said electronic signal.

3. A method according to claim 2, wherein magnetic diffusion weighted field gradients are applied in at least two different directions and the signals from the respective resultant resonances are subtracted to produce said discrimination of water diffusion anisotropy.

4. A method according to claim 3, wherein said magnetic field gradients are applied in mutually substantially orthogonal directions.

5. A method according to any of claims 2-4, wherein a process to eliminate non-neural signals is applied during magnetic resonance imaging.

6. A method according to claim 5, wherein the process comprises suppression of resonance signals from fat.

7. A method according to claim 6, wherein said suppression is effected by chemical shift suppression.

8. A method according to claim 6, wherein said suppression is effected by selective water stimulation.

9. A method according to claim 5, wherein the process comprises magnetisation transfer.

10. A method according to any of claims 2-9, which method utilises proton magnetic resonance.

11. A method according to any of claims 2-10, wherein the image is a three dimensional image.

12. A method of diagnosis or physiological investigation comprising application to a subject of a method according to any preceding claim.

13. A method of sective imaging, the method comprising observing diffusion anisotropy by magnetic resonance.

14. An apparatus for imaging neural tissue of a subject, the appratus comprising means for subjecting part of the subject anatomy to magnetic resonance fields adapted to discriminate anisotropy of water diffusion, means for detecting magnetic resonance to produce an electronic signal in accordance with said resonance and means for producing an image of neural tissue from said electronic signal.

15. An apparatus according to claim 14, further comprising a coil for application of a radiofrequency field to said anatomical part and/or for detection of a resonance signal, wherein said coil is configured and dimensioned to fit closely over said anatomy part.

16. An apparatus according to claim 15, wherein said coil is a solenoid coil or surface coil and is configured and dimensioned to fit closely over a human limb, shoulder, chest, pelvic region, neck, or back.

17. An apparatus for selectively imaging neural tissue of a subject without use of intraneural control agents, the apparatus comprising means for subjecting part of the subject anatomy to magnetic resonance fields, means for detecting magnetic resonance to produce an electronic signal in accordance with said resonance and means for producing an image of neural tissue from said electronic signal so that in said image, a nerve or root or neural tract of interest can be visually differentiated from surrounding structures.

18. A magnetic resonance apparatus for selective imaging, the apparatus being adapted to discriminate diffusion anisotropy.

19. A method of imaging neural tissue, the method being substantially as hereinbefore described with reference to any one of the accompanying drawings.

20. An apparatus for imaging neural tissue, the apparatus being substantially as hereinbefore described with reference to any one of the accompanying drawings.

ABSTRACT

IMAGING APPARATUS AND METHOD

In an apparatus and method for imaging neural tissue, a part of anatomy of a subject is subjected to magnetic resonance imaging fields. The fields are adapted to discriminate water diffusion anisotropy. Resonance signals are processed to produce the required image.

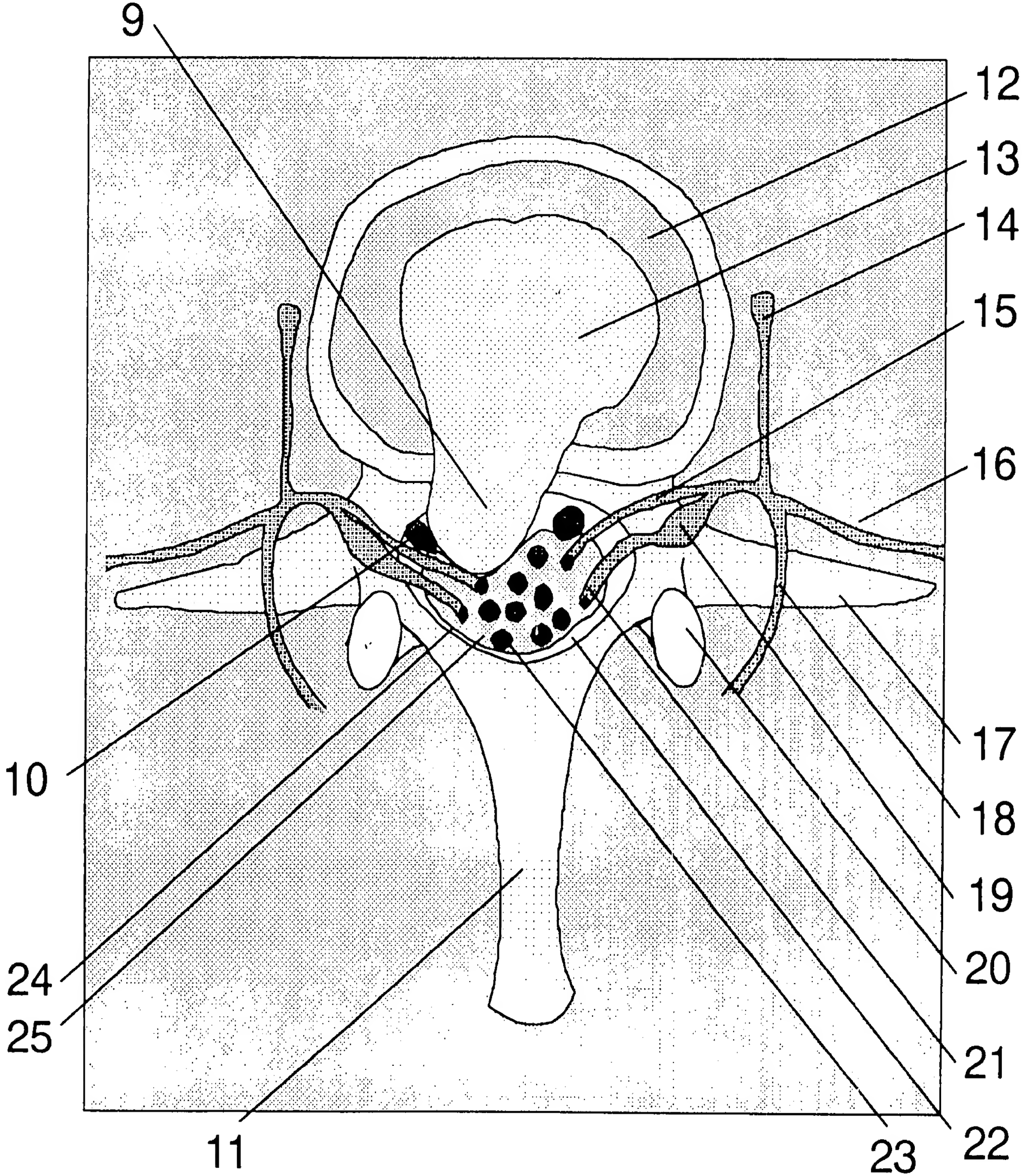


FIG 1

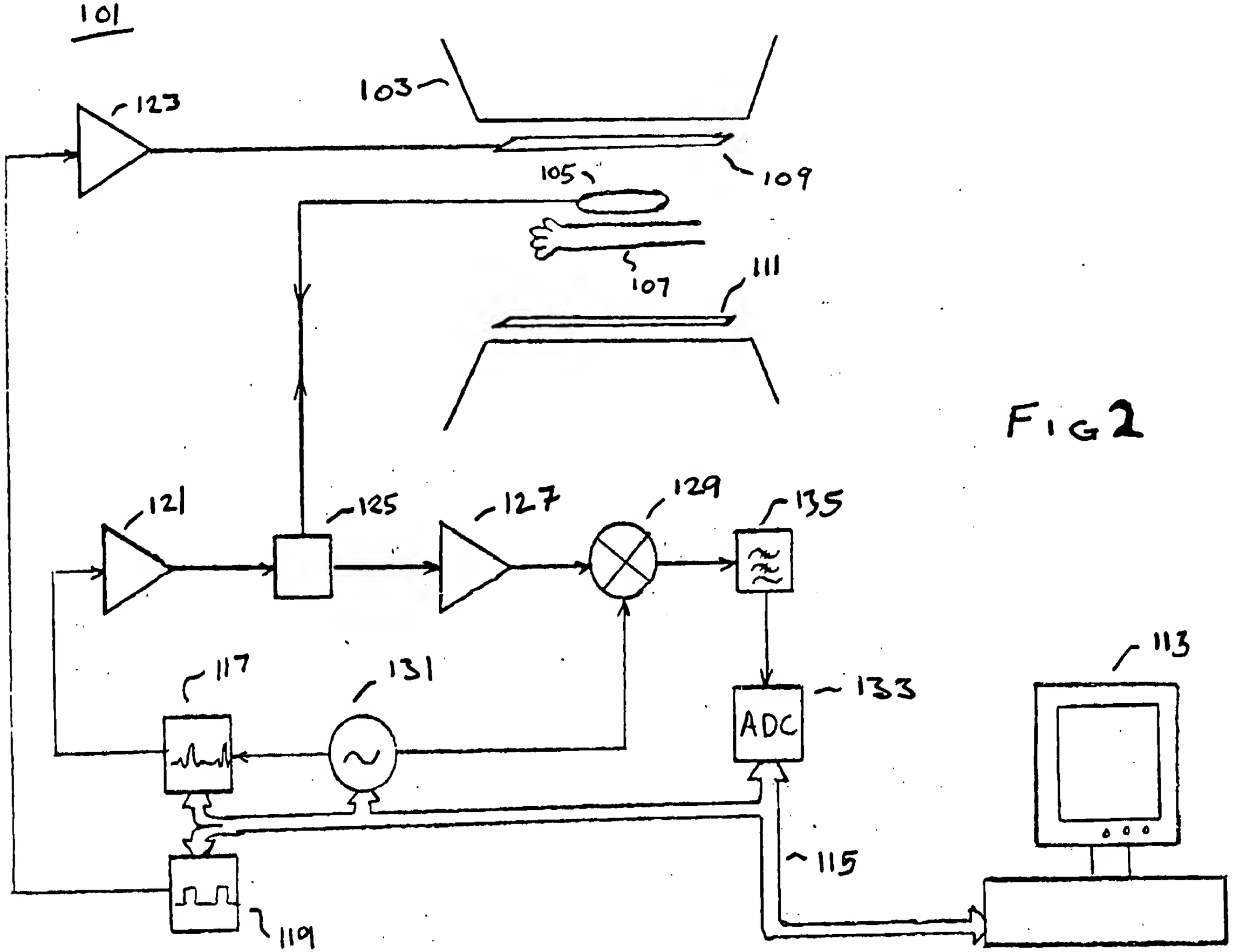
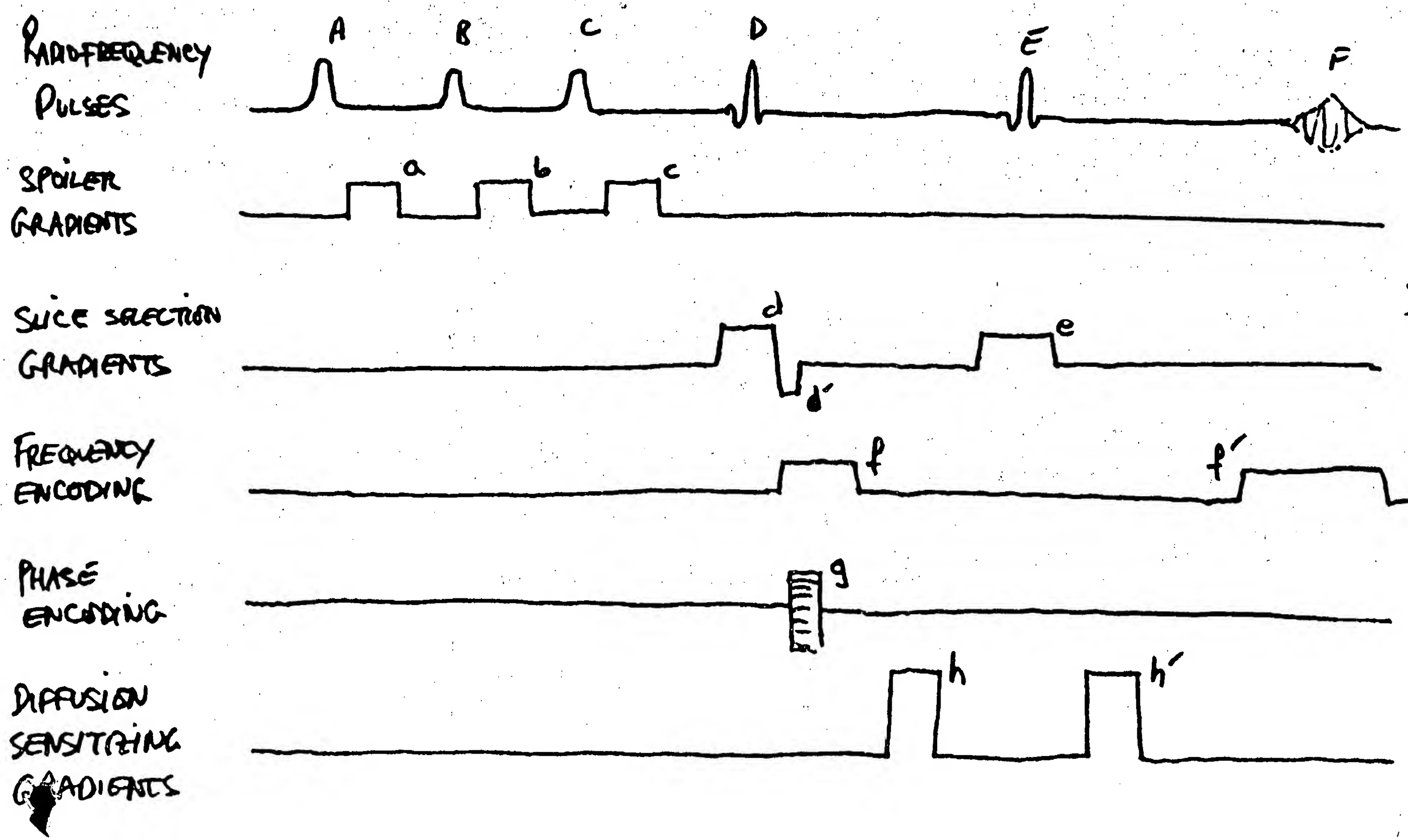

101
123
103
109
105
107
111
121
125
127
129
135
117
131
133
ADC
113
115
119

FIG 2

FIG 3


RADIOFREQUENCY PULSES
A
B
C
D
E
F
SPOILER GRADIENTS
a
b
c
SLICE SELECTION GRADIENTS
d
d'
e
FREQUENCY ENCODING
f
f'
PHASE ENCODING
g
DIFFUSION SENSITISING GRADIENTS
h
h'

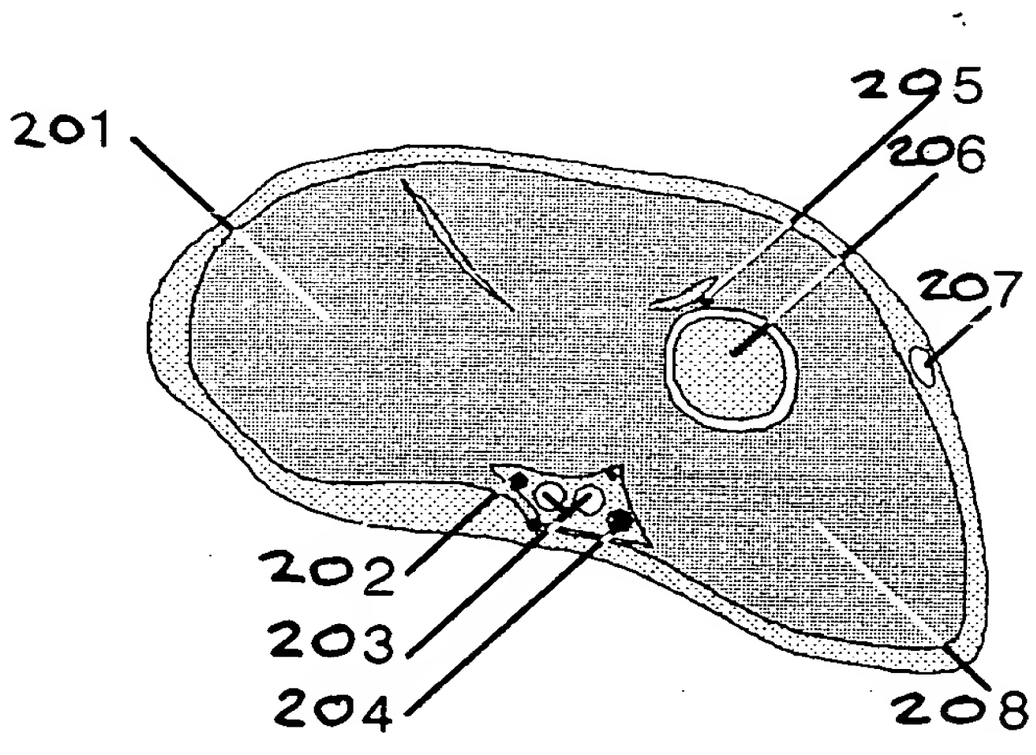


Figure 4

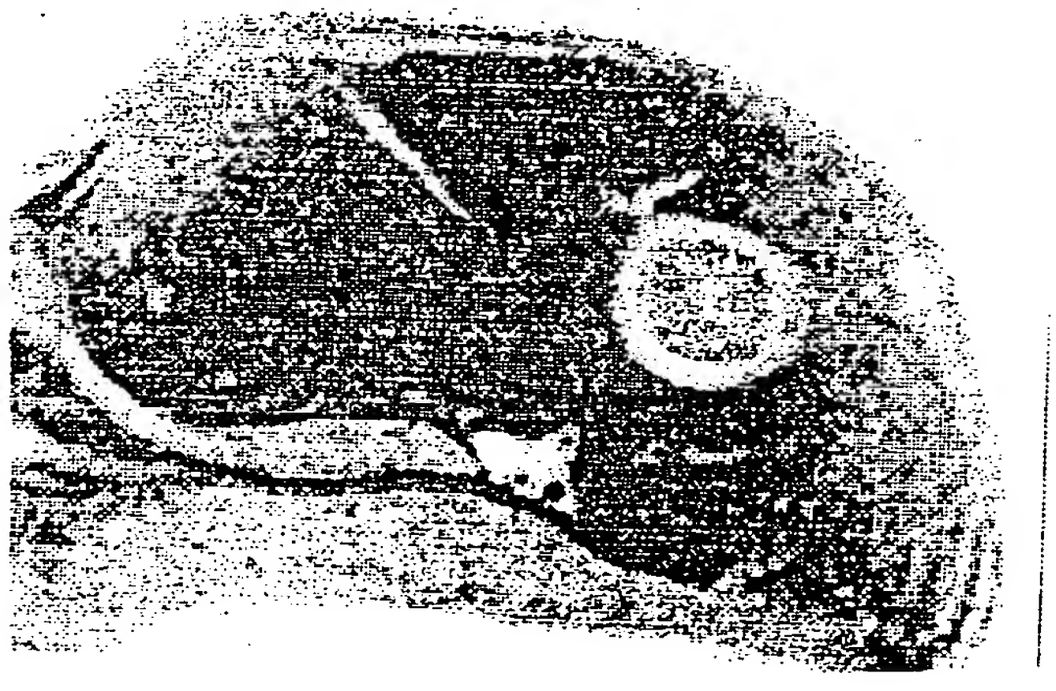


Figure 5

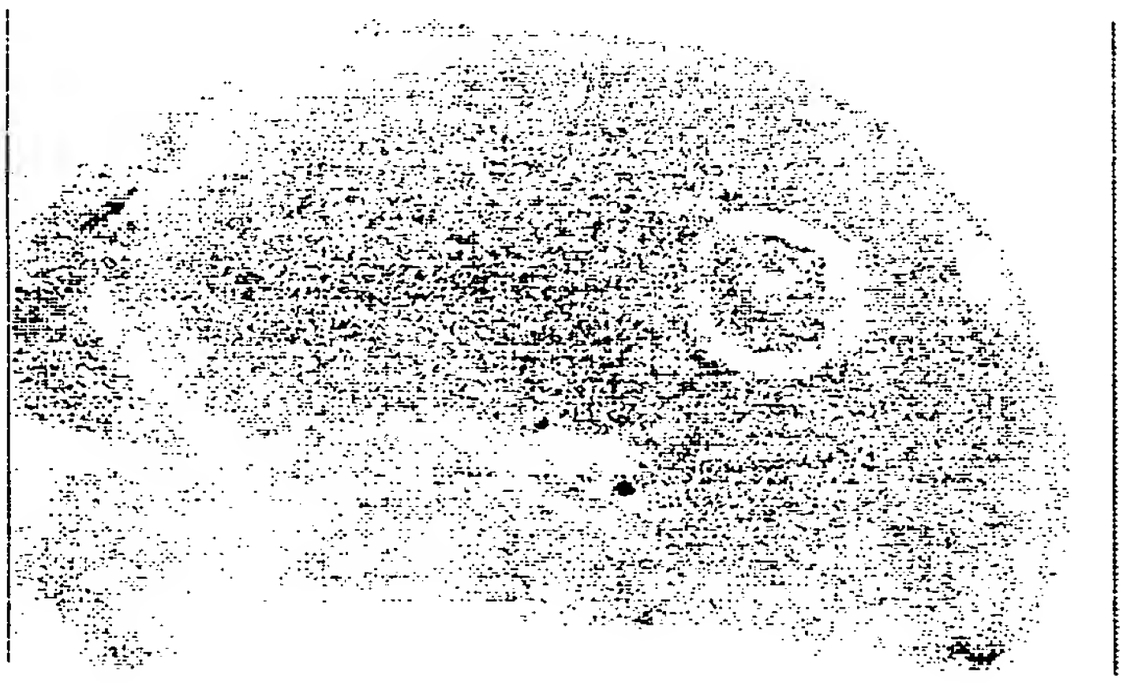


Figure 6

Figure 7